



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: February 20, 2009

To: NCCTG Primary Clinical Research Associates

From: Janis Wobschall
Protocol Development Coordinator

Re: N0572, A Phase I/II Study of Sorafenib and CCI-779 in Patients with Recurrent Glioblastoma

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with CCI-779 for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

AE_1803957

Please note that all risks currently cited in the NCCTG consent form cannot be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

Please submit this adverse event to your Institutional Review Board.

If you have any questions concerning this communication, please contact Janis Wobschall at wobschall.janis@mayo.edu or 507/284-4852.

JW/kjm
enclosure

IND SAFETY REPORT: INITIAL WRITTEN REPORT

TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA
Division of Drug Oncology Products, Center For Drug Evaluation and Research, FDA

FAX: 301-796-9849
301-796-9845

1. IND NUMBER 7921 61010	2. AGENT NAME Bevacizumab (rhuMab VEGF)(704865) CCI-779 (temsirolimus, ToriselTM)	3. DATE November 25, 2008
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4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, CTEP, DCTD, NCI L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI	6. PHONE NUMBER 301-496-1196	7. FAX NUMBER 301-402-0428
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8. PROTOCOL NUMBER (AE #)
GOG-0229G (AE# 1803957)

9. PATIENT IDENTIFICATION 004-0229G-003	10. AGE 54	11. SEX Female
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 54-year-old female with endometrioid endometrial adenocarcinoma who experienced a grade 4 hypomagnesemia while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. She began the investigational therapy on November 4, 2008, and received her first and last dose of bevacizumab (Cycle 1, Day 1) on that day and the last dose of temsirolimus on November 11, 2008 (Cycle 1, Day 8). On November 11, 2008, the patient presented to the clinic for Cycle 1, Day 8 investigational treatment with temsirolimus. She reported weakness, fatigue, and mild nausea. Her magnesium level drawn that day was 0.5 mg/dL (reference range: 1.5-2.5 mg/dL). Her baseline level drawn on October 24, 2008, was 1.8 mg/dL. On November 12, 2008, she received 4 gms of IV magnesium sulfate, and later that day her magnesium level had recovered to 1.9 mg/dL. She is due to return to the clinic for Cycle 1, Day 21 treatment on November 25, 2008. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE
Cycle =28 Days.
Temsirolimus 25 mg IV over 30 minutes on Days 1, 8, 15, and 22
Bevacizumab 10 mg/kg IV over 30-90 minutes on Days 1 and 15

14. DATES OF TREATMENT
The patient began the investigational therapy on November 4, 2008, and received the last dose of bevacizumab on November 4, 2008 (Cycle 1 Day 1), and temsirolimus on November 11, 2008 (Cycle 1, Day 8).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 18132, and for temsirolimus = 1374. There have been 30 other incidences of hypomagnesemia reported to the NCI through AdEERS as serious adverse events for bevacizumab; and no other incidences of hypomagnesemia reported to the NCI through AdEERS as a serious adverse event for temsirolimus.

COMMENTS
AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOW-UP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR312.32(d)(2).
DISCLAIMER per 21 CFR 312.32(e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB SENIOR INVESTIGATOR/ SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.